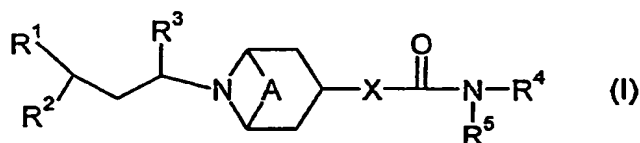


CLAIMS

1. A compound of formula (I):



5

wherein

A is absent or is (CH<sub>2</sub>)<sub>2</sub>;R<sup>1</sup> is C<sub>1-8</sub> alkyl, C(O)NR<sup>10</sup>R<sup>11</sup>, C(O)<sub>2</sub>R<sup>12</sup>, NR<sup>13</sup>C(O)R<sup>14</sup>, NR<sup>15</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, NR<sup>18</sup>C(O)<sub>2</sub>R<sup>19</sup>, heterocyclyl, aryl or heteroaryl;R<sup>10</sup>, R<sup>13</sup>, R<sup>15</sup>, R<sup>16</sup> and R<sup>18</sup> are hydrogen or C<sub>1-6</sub> alkyl;

10

R<sup>11</sup>, R<sup>12</sup>, R<sup>14</sup>, R<sup>17</sup> and R<sup>19</sup> are C<sub>1-8</sub> alkyl (optionally substituted by halo, hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkoxy, C<sub>3-6</sub> cycloalkyl (optionally substituted by halo), C<sub>5-6</sub>cycloalkenyl, S(C<sub>1-4</sub> alkyl), S(O)(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), heteroaryl, aryl,heteroaryloxy or aryloxy), aryl, heteroaryl, C<sub>3-7</sub> cycloalkyl (optionally substituted byhalo or C<sub>1-4</sub> alkyl), C<sub>4-7</sub> cycloalkyl fused to a phenyl ring, C<sub>5-7</sub> cycloalkenyl, or,

15

heterocyclyl (itself optionally substituted by oxo, C(O)(C<sub>1-6</sub> alkyl), S(O)<sub>k</sub>(C<sub>1-6</sub> alkyl),halo or C<sub>1-4</sub> alkyl); or R<sup>11</sup>, R<sup>12</sup>, R<sup>14</sup> and R<sup>17</sup> can also be hydrogen;or R<sup>10</sup> and R<sup>11</sup>, and/or R<sup>16</sup> and R<sup>17</sup> may join to form a 4-, 5- or 6-membered ring which optionally includes a nitrogen, oxygen or sulphur atom, said ring being optionally substituted by C<sub>1-6</sub> alkyl, S(O)<sub>k</sub>(C<sub>1-6</sub> alkyl) or C(O)(C<sub>1-6</sub> alkyl);

20

R<sup>2</sup> C<sub>1-6</sub> alkyl, phenyl, heteroaryl or C<sub>3-7</sub> cycloalkyl;R<sup>3</sup> H or C<sub>1-4</sub> alkyl;R<sup>4</sup> is aryl or heteroaryl;R<sup>5</sup> is H or alkyl;X is CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH=CH, OCH<sub>2</sub> or S(O)<sub>n</sub>CH<sub>2</sub>;

25

n is 0, 1 or 2;

unless specified otherwise aryl, phenyl and heteroaryl moieties are independently

optionally substituted by one or more of halo, cyano, nitro, hydroxy, OC(O)NR<sup>20</sup>R<sup>21</sup>,NR<sup>22</sup>R<sup>23</sup>, NR<sup>24</sup>C(O)R<sup>25</sup>, NR<sup>26</sup>C(O)NR<sup>27</sup>R<sup>28</sup>, S(O)<sub>2</sub>NR<sup>29</sup>R<sup>30</sup>, NR<sup>31</sup>S(O)<sub>2</sub>R<sup>32</sup>,C(O)NR<sup>33</sup>R<sup>34</sup>, CO<sub>2</sub>R<sup>36</sup>, NR<sup>37</sup>CO<sub>2</sub>R<sup>38</sup>, S(O)<sub>q</sub>R<sup>39</sup>, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl,

30

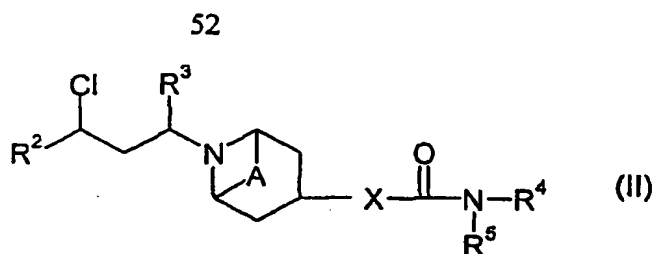
C<sub>3-10</sub> cycloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> alkoxy(C<sub>1-6</sub>)alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkoxy, phenyl, phenyl(C<sub>1-4</sub>)alkyl, phenoxy, phenylthio, phenylS(O), phenylS(O)<sub>2</sub>, phenyl(C<sub>1-</sub>

<sub>4</sub>alkoxy, heteroaryl, heteroaryl(C<sub>1-4</sub>)alkyl, heteroaryloxy or heteroaryl(C<sub>1-4</sub>)alkoxy;  
 wherein any of the immediately foregoing phenyl and heteroaryl moieties are  
 optionally substituted with halo, hydroxy, nitro, S(C<sub>1-4</sub> alkyl), S(O)(C<sub>1-4</sub> alkyl),  
 S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>NH<sub>2</sub>, S(O)<sub>2</sub>NH(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>N(C<sub>1-4</sub> alkyl)<sub>2</sub>, cyano, C<sub>1-4</sub>  
 5 alkyl, C<sub>1-4</sub> alkoxy, C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl), C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub>, CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-4</sub>  
 alkyl), NHC(O)(C<sub>1-4</sub> alkyl), NHS(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), CF<sub>3</sub> or OCF<sub>3</sub>;  
 unless otherwise stated heterocyclyl is optionally substituted by C<sub>1-6</sub> alkyl [optionally  
 substituted by phenyl {which itself optionally substituted by halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub>  
 alkoxy, cyano, nitro, CF<sub>3</sub>, OCF<sub>3</sub>, (C<sub>1-4</sub> alkyl)C(O)NH, S(O)<sub>2</sub>NH<sub>2</sub>, C<sub>1-4</sub> alkylthio,  
 10 S(O)(C<sub>1-4</sub> alkyl) or S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl)} or heteroaryl {which itself optionally substituted  
 by halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, cyano, nitro, CF<sub>3</sub>, (C<sub>1-4</sub> alkyl)C(O)NH, S(O)<sub>2</sub>NH<sub>2</sub>, C<sub>1-4</sub>  
 alkylthio, S(O)(C<sub>1-4</sub> alkyl) or S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl)}], phenyl {optionally substituted by  
 halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, cyano, nitro, CF<sub>3</sub>, OCF<sub>3</sub>, (C<sub>1-4</sub> alkyl)C(O)NH, S(O)<sub>2</sub>NH<sub>2</sub>,  
 C<sub>1-4</sub> alkylthio, S(O)(C<sub>1-4</sub> alkyl) or S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl)}, heteroaryl {optionally substituted  
 15 by halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, cyano, nitro, CF<sub>3</sub>, (C<sub>1-4</sub> alkyl)C(O)NH, S(O)<sub>2</sub>NH<sub>2</sub>, C<sub>1-4</sub>  
 alkylthio, S(O)(C<sub>1-4</sub> alkyl) or S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl)}, S(O)<sub>2</sub>NR<sup>40</sup>R<sup>41</sup>, C(O)R<sup>42</sup>, C(O)<sub>2</sub>(C<sub>1-6</sub>  
 alkyl) (such as tert-butoxycarbonyl), C(O)<sub>2</sub>(phenyl(C<sub>1-2</sub> alkyl)) (such as  
 benzyloxycarbonyl), C(O)NHR<sup>43</sup>, S(O)<sub>2</sub>R<sup>44</sup>, NHS(O)<sub>2</sub>NHR<sup>45</sup>, NHC(O)R<sup>46</sup>,  
 NHC(O)NHR<sup>47</sup> or NHS(O)<sub>2</sub>R<sup>48</sup>, provided none of these last four substituents is linked  
 20 to a ring nitrogen;  
 k, l, p and q are, independently, 0, 1 or 2;  
 R<sup>20</sup>, R<sup>22</sup>, R<sup>24</sup>, R<sup>26</sup>, R<sup>27</sup>, R<sup>29</sup>, R<sup>31</sup>, R<sup>33</sup>, R<sup>37</sup> and R<sup>40</sup> are, independently, hydrogen or C<sub>1-6</sub>  
 alkyl;  
 R<sup>21</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>28</sup>, R<sup>30</sup>, R<sup>32</sup>, R<sup>34</sup>, R<sup>36</sup>, R<sup>38</sup>, R<sup>39</sup>, R<sup>41</sup>, R<sup>42</sup>, R<sup>43</sup>, R<sup>44</sup>, R<sup>45</sup>, R<sup>46</sup>, R<sup>47</sup> and R<sup>48</sup>  
 25 are, independently, C<sub>1-6</sub> alkyl (optionally substituted by halo, hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub>  
 haloalkoxy, C<sub>3-6</sub> cycloalkyl, C<sub>5-6</sub> cycloalkenyl, S(C<sub>1-4</sub> alkyl), S(O)(C<sub>1-4</sub> alkyl),  
 S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), heteroaryl, phenyl, heteroaryloxy or phenyloxy), C<sub>3-7</sub> cycloalkyl,  
 phenyl or heteroaryl; wherein any of the immediately foregoing phenyl and heteroaryl  
 moieties are optionally substituted with halo, hydroxy, nitro, S(C<sub>1-4</sub> alkyl), S(O)(C<sub>1-4</sub>  
 30 alkyl), S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>NH<sub>2</sub>, S(O)<sub>2</sub>NH(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>N(C<sub>1-4</sub> alkyl)<sub>2</sub>, cyano,  
 C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl), C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub>, CO<sub>2</sub>H,  
 CO<sub>2</sub>(C<sub>1-4</sub> alkyl), NHC(O)(C<sub>1-4</sub> alkyl), NHS(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), C(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub> or  
 OCF<sub>3</sub>;

$R^{21}$ ,  $R^{23}$ ,  $R^{25}$ ,  $R^{28}$ ,  $R^{30}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{41}$ ,  $R^{42}$ ,  $R^{43}$ ,  $R^{44}$ ,  $R^{45}$ ,  $R^{46}$  and  $R^{47}$  may additionally be hydrogen;

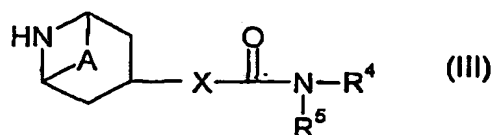
or a pharmaceutically acceptable salt thereof or a solvate thereof.

- 5 2. A compound as claimed in claim 1 wherein A is absent.
3. A compound as claimed in claim 1 or 2 wherein  $R^1$  is piperidinyl or piperazinyl substituted by  $S(O)_2C_{1-4}$  alkyl,  $S(O)_2C_{1-4}$  haloalkyl or  $C(O)NH$ -phenyl.
- 10 4. A compound as claimed in claim 1 or 2 wherein  $R^1$  is phenyl substituted by  $S(O)_2C_{1-4}$  alkyl.
5. A compound as claimed in claim 1, 2 or 3 wherein  $R^2$  is phenyl optionally substituted by 0, 1 or 2 fluorines.
- 15 6. A compound as claimed in claim 1, 2, 3, 4 or 5 wherein  $R^3$  is hydrogen.
7. A compound as claimed in any one of the preceding claims wherein  $R^4$  is phenyl or benzyl, either of which is optionally substituted by halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy,  $S(O)_z(C_{1-4}$  alkyl), nitro, cyano or  $CF_3$ ; wherein z is 0, 1 or 2.
- 20 8. A compound as claimed in any one of the preceding claims wherein  $R^5$  is hydrogen.
9. A compound as claimed in any one of the preceding claims wherein X is  $CH_2$  or  $CH=CH$ .
- 25 10. A compound of formula (I) as claimed in claim 1 can be prepared by:
  - a. for a compound of the invention wherein  $R^1$  is an N-linked optionally substituted heterocycle, reacting a compound of formula (II):

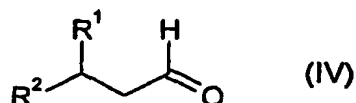


wherein  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , A and X are as defined in claim 1, with a compound  $R^1H$  (wherein the H is on a heterocycle ring nitrogen atom) wherein  $R^1$  is as defined in claim 1, in the presence of a suitable base, in a suitable solvent;

- 5      b. for a compound of the invention wherein  $R^3$  is hydrogen, coupling a compound of formula (III):

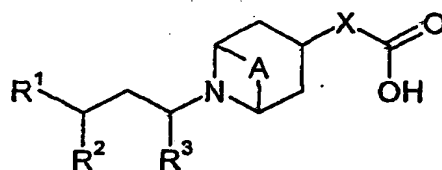


wherein  $R^4$ ,  $R^5$ , A and X are as defined in claim 1, with a compound of formula (IV):



10      wherein  $R^1$  and  $R^2$  are as defined in claim 1, in the presence of  $NaBH(OAc)_3$  (wherein Ac is  $C(O)CH_3$ ) in a suitable solvent at room temperature;

- c. activating the acid group of a compound of formula (V)



- 15      wherein X, A,  $R^1$ ,  $R^2$  and  $R^3$  are as defined in claim 1, and coupling the product so formed with an amine  $R^4R^5NH$  (wherein  $R^4$  and  $R^5$  are as defined in claim 1).

11.      A pharmaceutical composition which comprises a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, and a pharmaceutically acceptable adjuvant, diluent or carrier.
- 20

12. A compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, for use as a medicament.
13. A compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, in the manufacture of a medicament for use in therapy.
14. A method of treating a CCR5 mediated disease state comprising administering to a patient in need of such treatment an effective amount of a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof.